OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)
ASSISTANT SECRETARY OF THE NAVY (M&RA)
ASSISTANT SECRETARY OF THE AIR FORCE (M&RA)
DIRECTOR, JOINT STAFF

SUBJECT: Policy for Department of Defense Stockpile of Pentetate Calcium Trisodium Injection and Pentetate Zinc Trisodium Injection

This memorandum supersedes "Policy for Department of Defense Stockpile of Pentetate Calcium Trisodium Injection and Pentetate Zinc Trisodium Injection" dated February 25, 2009 (Health Affairs 9-005). The policy addresses the Department of Defense (DoD) Pentetate Calcium Trisodium (Ca-DTPA) and Pentetate Zinc Trisodium (Zn-DTPA) Injections stockpile for the treatment of individuals internally contaminated by the effects of a Radiological Dispersal Device or Improvised Nuclear Device. The U.S. Food and Drug Administration approved Ca-DTPA and Zn-DTPA for the treatment of individuals with known or suspected internal contamination with the transuranic elements plutonium, americium, or curium. These products augment existing DoD medical consequence management capability.

The attachment provides updated guidelines for the use of these radiation medical countermeasures. The point of contact for this issue is Colonel Keith Vesely, who can be reached at (703) 845-3310, or Keith.Vesely@ha.osd.mil.

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Performing the Duties of the Assistant Secretary of Defense (Health Affairs)

Attachment:
As stated

HA POLICY: 10-004

cc:
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force
Director, Health and Safety, U.S. Coast Guard
Director, Defense Logistics Agency

Health Affairs Policy for Use of Department of Defense Stockpile of Pentetate Calcium Trisodium Injection or Pentetate Zinc Trisodium Injection for the Treatment of Individuals Internally Contaminated By the Effects of a Radiological Dispersal Device or Improvised Nuclear Device

The Department of Defense (DoD) established an initial stockpile of Pentetate Calcium Trisodium Injection (Ca-DTPA) and Pentetate Zinc Trisodium Injection (Zn-DTPA) intravenous medications for the treatment of individuals internally contaminated by the effects of a Radiological Dispersal Device (RDD) or Improvised Nuclear Device (IND). The U.S. Food and Drug Administration (FDA) approved Ca-DTPA and Zn-DTPA as medical countermeasures for the treatment of individuals with known or suspected internal contamination with the transuranic elements plutonium (Pu), americium (Am), or curium (Cm) to increase the rates of elimination. Ca-DTPA and Zn-DTPA augment existing DoD medical consequence management capability.

The use of Ca-DTPA and Zn-DTPA at military facilities shall be consistent with the Department of Health and Human Services (HHS) Radiation Event Medical Management guidelines, (http://www.remm.nlm.gov/index.html). The Assistant Secretary of Defense for Health Affairs (ASD(HA)) will review this policy upon any future revision of HHS guidance on the use of Ca-DTPA or Zn-DTPA.

BACKGROUND

United States military personnel, their families, U.S. Government civilian workers, and U.S. Government contractors may be at risk from terrorist use of transuranic metals as components of an RDD or "dirty bomb." Terrorists might use Pu as the fissile material in an IND. Risks from such radioactive materials include contamination and exposure, externally and internally. In cases where prevention of internal contamination has failed, victims may take in radioactive material through inhalation, ingestion, open wounds, or burns. Various factors, including the chemical form of the isotope and the pathway of absorption, may influence the treatment method and effectiveness of internal radioisotope removal. Such treatment may include recapture of the radioactive metals through binding with a chelator (i.e., binding agent). Chelation (i.e., binding) involves the formation of stable ionic complexes for elimination from the body in urine. Ca-DTPA and Zn-DTPA form less stable chelates with uranium and neptunium *in vivo* resulting in the deposition of these elements in tissues including the bone. Ca-DTPA and Zn-DTPA treatments are not effective for uranium and neptunium. For clarification, Ca-DTPA and Zn-DTPA do not bind with radioactive isotopes such as iodine or cesium.

STOCKPILES

Military medical treatment facility (MTF) commanders shall evaluate the RDD and IND threat to their supported population and, if a threat exists, consider holding a

small quantity of Ca-DTPA and Zn-DTPA on-hand. MTFs shall be prepared to function independently for up to the first 48 hours of an event.

ASD(HA) acquired and will pre-position stockpiles of Ca-DTPA and Zn-DTPA at Theater Lead Agents for Medical Materiel, Defense Distribution Depots, and those Medical Materiel facilities specifically designated by the GCC (hereafter referred to as "GCC storage location(s)") (see Table 1).

ASD(HA) will retain a small quantity of Ca-DTPA and Zn-DTPA at Defense Distribution Depot Susquehanna (DDSP) to serve as the fly-away package for radiological medical specialty teams (e.g., a U.S. Army Radiological Advisory Medical Team (RAMT)).

Table 1: GCC Storage Locations

GCC	GCC STORAGE LOCATION(S)	NOTES
USAFRICOM	U.S. Army Medical Materiel Center Europe (USAMMCE)	
USCENTCOM	U.S. Army Medical Materiel Center – South West Asia	
USEUCOM	USAMMCE	
USNORTHCOM	Brooke Army Medical Center	
USPACOM	TLAMM-Pacific, U.S. Army Medical Materiel Center-Korea, Defense Distribution Depot Yokosuka Japan	Three locations are required to support forces throughout the region.
USSOUTHCOM	KellyUSA	

RELEASE AUTHORITY

Materiel purchased by the MTF is for use by that facility and its subordinate or supported units or facilities. Authority to release this supply of Ca-DTPA and Zn-DTPA is vested in the MTF Commander, who retains operational control of these radiation medical countermeasures. Operational decisions regarding use of this supply will be consistent with the priorities for Ca-DTPA and Zn-DTPA use presented in this policy, in addition to current clinical guidelines by cognizant public health specialists and organizations, and the FDA-approved product labels.

ASD(HA) designates the commander of each GCC as release authority for the ASD(HA)-acquired Ca-DTPA and Zn-DTPA stored within each respective GCC area of responsibility.

ASD(HA) will retain control of any remaining materiel stored at DDSP and will coordinate with Joint Staff and Defense Supply Center Philadelphia (DSCP) if such materiel is used as a radiological medical specialty team fly-away package.

For pre-event distribution, Ca-DTPA and Zn-DTPA will be shipped from GCC storage locations using standard medical logistics supply chain processes, or, if required, alternate GCC-directed means (e.g., military ground or air transport). For post-event distribution, Ca-DTPA and Zn-DTPA will be shipped from GCC storage locations using standard life-or-death medical logistics supply chain processes, or, if required, alternate GCC-directed means (e.g., military ground or air transport), as the products are most effective when administered immediately and up to the first 24 hours after internal contamination with the transuranic elements Pu, Am, and Cm. The associated costs shall be paid by the GCC in all cases.

The GCC should evaluate the threat of release of the transuranics Pu, Am, and Cm, and develop plans to treat individuals and to receive, store, maintain, and rapidly distribute Ca-DTPA and Zn-DTPA for treatment of appropriately selected casualties. Treatment with Ca-DTPA or Zn-DTPA should not begin without approval of the Command Surgeon or Public Health Emergency Officer when there is clinical diagnosis or suspected occurrence of internal contamination with these radioactive metals.

SCREENING AND ASSESSMENT

All potential casualties must be screened for external radioactive contamination to determine if they have a possibility for internal contamination. External screening shall be accomplished with appropriate instrumentation capable of detecting low energy gamma emissions with particular attention given to monitoring the upper body, especially for contamination of the head, hair, and shoulders. The resulting high-risk subpopulation should be medically evaluated. Presumptive casualties potentially requiring chelation treatment consist of two groups. The first group includes individuals near ground-zero or in the close (high zone) downwind plume footprint processed through controlled exits. The second potential high-risk group includes those individuals in the high exposure (high zone) areas but who escaped contamination screening at an exit point or triage site (unscreened). Individuals presenting at the controlled exits of guided evacuation routes, or at triage points must be screened for potentially contaminated wounds or upper body contamination, and triaged accordingly. The resulting known or suspected positives from all potential casualties whether screened at controlled exits or at another site and time should be treated as soon as possible, pending diagnostic testing to determine their need for continuation of therapy.

INDICATIONS AND USAGE

For indications and usage, dosage and administration guidelines, and laboratory testing and monitoring information of Ca-DTPA and Zn-DTPA, see Appendices 1 and 2, respectively. These attachments are the product inserts and describe the FDA-approved use of the two chelators.

COLLECTION OF PATIENT TREATMENT DATA

Clinical staff will complete an Armed Forces Radiobiology Research Institute (AFRRI) Biodosimetry Worksheet for each patient treated to assist the health care provider in determining the duration of treatment. The worksheets are available from the Biodosimetry Tools section of the AFRRI website (http://www.afrri.usuhs.mil/outreach/biodostools.htm#forms). Forward the completed forms to the patient medical record custodians.

Clinical staff should complete the Ca-DTPA manufacturer Patient Treatment Form or the Zn-DTPA manufacturer Patient Treatment Form for each patient treated, subject to operational constraints. The manufacturer requests the information to develop long-term response data and information on the risk of developing late malignancy. Mail completed forms to: Hameln Pharmaceuticals GMBH, Langes Feld 13, 31789 Hameln, Germany. The forms are available from the U.S. commercial distributor's website (http://www.akorn.com/dtpa_product_info.php).

RADIOLOGICAL MEDICAL SPECIALTY TEAMS

The DoD has radiological medical specialty teams available to assist the GCC in response to events of the type described in this policy (e.g., AFRRI Medical Radiobiology Advisory Teams and U.S. Army RAMTs). The teams have various capabilities, including providing health physics, medical, and radiobiological advice to military and civilian command and control operations; evaluating radiation hazards; advising on contamination control, radiation exposure risks, and protective action guidelines. A U.S. Army RAMT can provide limited medical support. The teams are deployable and, through "reachback," can call on the knowledge and skills of radiobiologists, biodosimetrists, and other research professionals. Use of the teams' expertise in planning and response is strongly encouraged.

LOGISTICS CONSIDERATIONS

Inventory Management: All Ca-DTPA and Zn-DTPA inventory shall be tracked and accounted for at each GCC storage location and the MTF storage locations using existing Service and Joint medical logistics automated information systems (AIS) (e.g., Defense Medical Logistics Standard Support). Inventory managers will ensure that on-hand balances and quality assurance information are entered into their respective medical logistics AIS and that the AIS are reporting the data to the Joint Medical Asset Repository (JMAR). The JMAR will provide this data to the ASD(HA) Force Health Protection & Readiness Chemical, Biological, Radiological, and Nuclear Defense Medical Materiel Dashboard.

Storage and Shipping Requirements: The temperature requirement for Ca-DTPA and Zn-DTPA, as defined on the product labels, is 15 - 30°C (59 - 86°F). Exposures

outside the required storage temperatures could cause the product to lose efficacy, could lead to product adulteration that could threaten patient safety, or could lessen shelf life. Both products shall be transported, stored, and handled in accordance with the guidance provided on the product label and in the United States Pharmacopeia (USP), Chapter 1079, Good Storage and Transportation Standard. The USP is the U.S. standard for the storage and handling of finished pharmaceutical products. Appropriate shipping procedures and containers shall be used to maintain required temperature range during transit and temperatures will be monitored during transport by placing electronic time and tracking temperature devices in every container, in accordance with local cold chain/thermal management standard operating procedures.

Security: The integrity of the medical logistics supply chain must remain secure. The risk to the product is that it will be diverted by those seeking monetary gain or by those who fear they will not receive treatment. The use of electronic track and trace technology (e.g., Radio Frequency Identification) is encouraged.

Shelf Life/Expiration Dates: The ASD(HA)-acquired Ca-DTPA and Zn-DTPA each consists of a single lot, and so each has a single expiration date. The product has a 10-year shelf life from time of manufacture when stored and transported at the temperatures defined on the product labels. The lot numbers and expiration dates for the ASD(HA) stockpiled materiel are in Table 2.

Shelf Life Extension: Ca-DTPA and Zn-DTPA are not entered in the DoD/FDA Shelf Life Extension Program (SLEP). ASD(HA) is exploring SLEP eligibility for both products and will provide guidance at a future date.

Associated Supplies: The majority of the supplies needed are commonly present in existing MTFs (e.g., needles, syringes, intravenous sets, and blood/urine collection supplies). If Ca-DTPA or Zn-DTPA is pushed from a GCC storage location or MTF to a treatment team or smaller MTF, or if treatment is conducted outside MTFs (e.g., gymnasium, tent), all required supplies may not be available. MTF commanders and the GCC storage location will coordinate with the supported MTFs or medical response teams to determine the identity and quantity of associated supplies necessary to initiate and sustain treatment with Ca-DTPA and Zn-DTPA, will develop kits of associated supplies as required, and will ensure that these kits and the Ca-DTPA and Zn-DTPA are delivered simultaneously. The GCC will fund the costs for the associated supplies.

RESUPPLY AND REPLENISHMENT

Resupply During a Contingency (e.g., Response to an RDD or IND): MTFs in the U.S. and its territories shall coordinate for resupply with Local, Territorial, and State Strategic National Stockpile Coordinators. MTFs outside the U.S. and its territories shall requisition materiel from their supporting GCC storage location. National Stock

Numbers & National Drug Codes for each product are in Table 2, additional logistics data is in Tables 3 and 4.

Replenishment of MTF-acquired Materiel: Replenishment of MTF-acquired materiel is the responsibility of the Services and MTFs. GCC storage locations shall not use the ASD(HA)-acquired stockpile materiel to replenish MTFs.

Replenishment of ASD(HA)-acquired Ca-DTPA and Zn-DTPA Stockpile at GCC Storage Locations: The ASD(HA) purchased Ca-DTPA and Zn-DTPA to ensure immediate access in an RDD or IND event. Replenishment following use of the ASD(HA)-acquired materiel or replacement when it expires is the responsibility of the GCC.

Table 2: Product Identification, Lot Numbers, and Expiration Dates

Product	Description	National Stock Number (NSN)	National Drug Code (NDC)	Lot Number	Expiration Date
Ca-DTPA	200 mg/mL single use ampoules	6505-01-526-6210	52919-001-03	641060	31-Oct-16
Zn-DTPA	200 mg/mL single use ampoules	6505-01-526-6547	52919-002-03	R446060	30-Nov-14

Table 3: Logistics Data

Description	Size of Ampoule	Ampoule Strength	Unit of Sale	Intermediate Package	Case
200 mg/mL single use glass ampoules (amps)	5 mL	1000 mg (1 gram)	Box of 10 amps	10 Boxes Shrink-wrapped (1 Bundle)	10 Bundles

Table 4: Manufacturer, Distributor, Case Weight and Dimensions

Manufacturer	Distributor	Case Dimension	Case Wt
Hameln Pharmaceuticals	Akorn	515 mm high x 380 mm wide x 207 mm deep (8.15" x 20.28" x 14.96")	13 kg (28.7 lbs)